IN THE CLAIMS:

The status of each claim that has been introduced in the above-referenced application is identified in the ensuing listing of the claims. This listing of the claims replaces all previously submitted claims listings.

1. (Currently amended) A biomolecular substrate comprising:

a core molecular backbone comprising means for assaying for enzymes or substrates; and

a means for detection comprising a dissociatable, ground state-quenched intramolecular dimer including:

a first means for fluorescent ~~dye~~ labeling covalently attached to said core molecular backbone; and

a second ~~dye~~ means for labeling covalently attached to said ~~core molecular backbone~~means for assaying for enzymes or substrates which, when said biomolecular substrate is not covalently modified and said second means for labeling remains a part of said dimer, ~~physically associates with said first fluorescent dye forming a ground state-quenched intramolecular dye dimer,~~ fluorescence of ~~which~~ said first means for fluorescent labeling is at least partially quenched through a non-fluorescence resonance energy transfer mechanism, but which, when said biomolecular substrate is covalently modified without being cleaved, said second means for labeling physically dissociates from said first means for fluorescent ~~dye~~ labeling, resulting in dequenching of at least ~~one of~~ said first means for fluorescent labeling~~and second fluorescent dyes~~.

2. (Currently amended) The biomolecular substrate of claim 1, wherein said second ~~dye is a~~ means for labeling comprises means for fluorescent ~~dye~~labeling.

3. (Currently amended) The biomolecular substrate of claim 1, further comprising a first ~~spacer segment~~ means for spacing included at a first terminus of said ~~core molecular backbone~~means for assaying for enzymes or substrates.

4. (Currently amended) The biomolecular substrate of claim ~~1~~3, further comprising ~~a first spacer segment included at a first terminus of said core molecular backbone and~~ a second ~~spacer segment~~ means for spacing included at a second terminus of said ~~core molecular backbone~~means for assaying for enzymes or substrates.

5. (Currently amended) The biomolecular substrate of claim 1, wherein said first means for fluorescent ~~dye~~ labeling is selected from a group consisting of fluorescein, rhodamine, cyanine, Oregon Green, Texas Red, Lucifer Yellow, BODIPY, rhodol, coumarin, pyrene, eosin, erythrosin, napthalene, pyridyloxazole, anthrancene, fluorescamine, acridine, benzofuran, anthranilic acid, aminobenzoic acid, N-methylisatoic acid, isoluminol, bezoxadiazole, carboxybenzoyl-quinoline-carboxyaldehyde, salicylate, bimane, phenathroline, Yellow Fluorescent Protein, and Green Fluorescent Protein.

6. (Currently amended) The biomolecular substrate of claim 1, wherein said second ~~dye~~ means for labeling is selected from a group consisting of fluorescein, rhodamine, cyanine, Oregon Green, Texas Red, Lucifer Yellow, BODIPY, rhodol, coumarin, pyrene, eosin, erythrosin, napthalene, pyridyloxazole, anthrancene, fluorescamine, acridine, benzofuran, anthranilic acid, aminobenzoic acid, N-methylisatoic acid, isoluminol, bezoxadiazole, carboxybenzoyl-quinoline-carboxyaldehyde, salicylate, bimane, phenathroline, Yellow Fluorescent Protein, and Green Fluorescent Protein.

7. (Currently amended) The biomolecular substrate of claim 1, wherein said ~~core molecular backbone~~means for assaying for enzymes or substrates comprises ~~a molecule selected from a group consisting of~~ at least one of a peptide, a protein, a nucleic acid, a sugar, a lipid, a receptor, and a biopolymer.

8. (Canceled)

9. (Canceled)

10. (Currently amended) The biomolecular substrate of claim 1, wherein said ~~core molecular backbone~~means for assaying for enzymes or substrates includes at least one amino acid configured for phosphorylation by ~~includes~~ a protein kinase ~~substrate~~.

11. (Canceled)

12. (Canceled)

13. (Canceled)

14. (Currently amended) The protein kinase substrate of claim 1, wherein ~~the core molecular backbone~~ said means for assaying for enzymes or substrates comprises a ~~KID~~ kinase-inducible domain peptide sequence of a cyclic adenosine monophosphate response element binding protein, ~~the~~ said first means for fluorescent ~~dye~~ labeling comprises 5-carboxyfluorescein-succinimidyl ester or 5-carboxytetramthylrhodamine, succinimidyl ester conjugated at an N-terminus of the kinase-inducible domain, and ~~the~~ said second ~~dye~~ means for fluorescent labeling comprises tetramethylrhodamine-5-maleimide linked to a cysteine residue of the means for assaying for enzymes or substrates.

15. (Currently amended) A method of assaying covalent biomolecular modification in a reaction comprising:

providing a sample with a biomolecular substrate comprising:

a core molecular backbone comprising means for assaying for enzymes or substrates; and

a means for detection comprising a dissociatable, ground state-quenched intramolecular dimer including:

a first means for fluorescent ~~dye~~ labeling covalently attached to said ~~core molecular backbone~~means for assaying for enzymes or substrates; and

a second ~~dye~~ means for labeling covalently attached to said ~~core molecular backbone~~ means for assaying for enzymes or substrates which, when said biomolecular substrate is not covalently modified and said second means for labeling remains a part of said dimer, ~~physically associates with said first fluorescent dye forming a ground state quenched intramolecular dye dimer,~~ fluorescence of ~~which~~ said first means for fluorescent labeling is at least partially quenched through a non-fluorescence resonance energy transfer mechanism, and affecting fluorescence or absorbance characteristics of said biomolecular substrate, but which dissociates from said first means for fluorescent ~~dye~~ labeling when said biomolecular substrate is covalently modified without being cleaved;

introducing said biomolecular substrate to said sample; and

quantifying a resultant change in said fluorescence or absorbance characteristics of said biomolecular substrate.

16. (Original) The method of claim 15, wherein said biomolecular substrate is introduced into said living cells.

17. (Original) The method of claim 15, wherein said sample includes a drug targeting a specific process of covalent biomolecular modification.

18. (Original) The method of claim 16, wherein said sample includes a drug targeting a specific process of covalent biomolecular modification.

19. (Original) The method of claims 15, wherein said step of providing a biomolecular substrate comprises providing two or more different biomolecular substrates, each of said two or more biomolecular substrates being specific for different processes of covalent biomolecular modification and having unique and distinguishable spectral properties.

20. (Original) The method of claim 16, wherein said step of providing a biomolecular substrate comprises providing two or more different biomolecular substrates, each of said two or more biomolecular substrates being specific for different processes of covalent biomolecular modification and having unique and distinguishable spectral properties.

21. (Original) The method of claim 15, wherein the step of quantifying the resultant change in said fluorescence or absorbance characteristics of said biomolecular substrate comprises quantifying the resultant change in fluorescence or absorbance of said biomolecular substrate without separating biomolecular substrate which has been covalently modified from biomolecular substrate which has not been covalently modified.

22. (Original) The method of claim 16, wherein the step of quantifying the resultant change in fluorescence or absorbance characteristics of said biomolecular substrate comprises quantifying the resultant change in fluorescence or absorbance of said biomolecular substrate without separating biomolecular substrate which has been covalently modified from biomolecular substrate which has not been covalently modified.

23. (Currently amended) A method of assaying protein kinase activity comprising:
providing a biomolecular substrate comprising:
a KID peptide sequence including means for assaying for enzymes or substrates; and
a means for detection including a dissociatable, ground state-quenched intramolecular dye dimer comprising:
a first ~~molecule~~ means for labeling comprising a fluorescein or a rhodamine; and
a second ~~molecule of~~ means for labeling comprising a rhodamine near the opposite end of said KID peptide sequence which, when said biomolecular substrate is not phosphorylated, physically associates with said first ~~molecule~~ means for labeling forming ~~an~~ said intramolecular dye dimer, fluorescence of which is at least partially quenched through a non-fluorescence resonance energy transfer mechanism, and physically

dissociates from said first molecule when said biomolecular substrate is phosphorylated by a protein kinase to reduce said non-fluorescence resonance energy-transfer quenching;

providing a sample;

introducing said protein kinase substrate to said sample; and

quantifying a resultant change in fluorescence or absorbance of said biomolecular substrate.

24. (Original) The method of claim 23, wherein the step of quantifying the resultant change in fluorescence or absorbance of said biomolecular substrate comprises quantifying the resultant change in fluorescence or absorbance of said biomolecular substrate without separating biomolecular substrate which has been phosphorylated from biomolecular substrate which has not been phosphorylated.

25. (Currently amended) A method of identifying substrates of novel enzymes which catalyze covalent structural modifications of particular proteins or peptide sequences comprising:

gathering a combinatorial library of unique double-labeled substrates, said unique double-labeled substrates each comprising:

a means for assaying for enzymes or substrates including a particular, randomized core amino acid sequence;

a first means for fluorescent ~~dye~~ labeling covalently attached to said particular, randomized core amino acid sequence; and

a second ~~dye~~ means for labeling covalently attached to said particular, randomized core amino acid sequence which, when said unique double-labeled substrates are not covalently modified, physically associates with said first fluorescent dye forming a quenched intramolecular dye dimer, fluorescence of which is at least partially quenched through a non-fluorescence resonance energy transfer mechanism, and affecting the fluorescence or absorbance characteristics of said unique double-labeled substrates, but which physically dissociates from said first fluorescent dye

when said unique double-labeled substrates are covalently modified without being cleaved;

systematically contacting each of said unique double-labeled substrates with a novel enzyme;

quantifying any change in fluorescence or absorbance characteristics of each of said unique double-labeled substrates;

selecting members of the library undergoing a fluorescence change or an absorbance change; and

determining the amino acid sequence of said selected members of the library.

26. (Currently amended) A kit comprising:

a container;

one or more different biomolecular substrates contained within said container, each of said one or more different biomolecular substrates comprising:

a core molecular backbone comprising a means for assaying for enzymes or substrates;

a first means for fluorescent ~~dye~~ labeling associated with said core molecular backbone;

a second ~~dye~~ means for labeling associated with said core molecular backbone which, when said biomolecular substrate is not covalently modified, physically associates with said first means for fluorescent ~~dye~~ labeling forming a non-fluorescent intramolecular dye dimer at least partially through a ground state quenching mechanism, but which physically dissociates from said first means for fluorescent ~~dye~~ labeling when said biomolecular substrate is catalytically or non-catalytically covalently modified without being cleaved to reduce quenching by said ground state interaction; and

a sample of enzyme standard with which to standardize the assay.

27. (Currently amended) A method of identifying substrates of novel enzymes which catalyze covalent structural modifications of particular nucleic acids comprising:

gathering a combinatorial library of unique double-labeled substrates, said unique double-labeled substrates each comprising:

a means for assaying for enzymes or substrates including a particular, randomized core nucleic acid sequence;

a first means for fluorescent ~~dye~~ labeling associated with said particular, randomized core nucleic acid sequence; and

a second ~~dye~~ means for labeling associated with said particular, randomized core nucleic acid sequence which, when said unique double-labeled substrates are not covalently modified, physically associates with said first means for fluorescent ~~dye~~ labeling forming a quenched intramolecular ~~dye~~ dimer, fluorescence of which is at least partially quenched through a non-fluorescence resonance energy transfer mechanism, and affecting the fluorescence or absorbance characteristics of said unique double-labeled substrates, but which physically dissociates from said first means for fluorescent ~~dye~~ labeling when said unique double-labeled substrates are covalently modified without being cleaved;

systematically contacting each of said unique double-labeled substrates with a novel enzyme;

quantifying any change in fluorescence or absorbance of each of said unique double-labeled substrates;

selecting members of the library undergoing a fluorescence or absorbance change; and

determining the nucleotide sequence of said selected members of the library.

28. (New) The biomolecular substrate of claim 10, wherein said means for assaying for substrates comprises a peptide.

29. (New) The biomolecular substrate of claim 10, wherein said means for assaying for enzymes or substrates comprises SEQ ID NO: 1 and is covalently modifiable by Ca^{2+}/calmodulin-dependent protein kinase II.

30. (New) The biomolecular substrate of claim 10, wherein said means for assaying for enzymes or substrates comprises SEQ ID NO: 2 and is covalently modifiable by Ca^{2+}/calmodulin-dependent protein kinase II.

31. (New) The biomolecular substrate of claim 10, wherein said means for assaying for enzymes or substrates comprises SEQ ID NO:3 and is covalently modifiable by mitogen-activated protein kinase.

32. (New) The biomolecular substrate of claim 10, wherein said means for assaying for enzymes or substrates comprises , SEQ ID NO: 4, and is covalently modifiable by insulin receptor protein-tyrosine kinase.

33. (New) The biomolecular substrate of claim 10, wherein said means for assaying for enzymes or substrates comprises SEQ ID NO: 9 and is covalently modifiable by Protein Kinase A and Protein Kinase C.

34. (New) The biomolecular substrate of claim 14, wherein said means for assaying for enzymes or substrates comprises SEQ ID NO: 5 and said kinase-inducible domain comprises SEQ ID NO: 7.

35. (New) The biomolecular substrate of claim 31, wherein said tetramethylrhodamine-5-maleimide is linked to a cysteine residue near a C-terminus of SEQ ID NO: 7.